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Irene J. Virgolini, M.D. is Chair of the Experimental Nuclear Medicine Unit at the Department of Nuclear Medicine, University of Vienna with her main emphasis on the conduction of clinical trials. Dr. Virgolini received her M.D. in 1987 from the University of Vienna, and has held the following appointments: Associate Professor of Experimental Nuclear Medicine, Specialist of Internal Medicine, Associate Professor of Internal Medicine and Specialist of Nuclear Medicine. Dr. Virgolini has over 200 publications; her research interests include the development of new diagnostic and therapeutic agents in nuclear medicine, receptor kinetics (*in vitro* and *in vivo*), gastrointestinal peptides and hormones, cytokines and cytokine receptors, arteriosclerosis and thrombosis.

Radiolabeled Lanreotide (^{90}Y-MAURITIUS) for Tumor Therapy

Background. The high level expression of somatostatin receptors (SSTR) on various tumor cells has provided the molecular basis for successful use of radiolabeled lanreotide as tumor tracer in nuclear medicine. The vast majority of human tumors seem to over-express the one or the other of five distinct hSSTR subtype receptors. For instance, neuroendocrine tumors seem to frequently over-express hSSTR2, whereas intestinal adenocarcinomas frequently over-express hSSTR3 or hSSTR4, or both of these hSSTR. In contrast to ^{111}In-DTPA-D-Phe^{1}-octreotide which binds to hSSTR2 and 5 with high affinity (K_d 0.1-5 nM), to hSSTR3 with moderate affinity (K_d 10-100 nM) and does not bind to hSSTR1 and 4, ^{111}In / ^{90}Y-DOTA-lanreotide binds to hSSTR2, 3, 4, and 5 with high affinity, and to hSSTR1 with lower affinity (K_d 200 nM). Based on its unique hSSTR binding profile, we have suggested ^{111}In-DOTA-lanreotide to be a potential radioligand for tumor diagnosis, and ^{90}Y-DOTA-lanreotide suitable for receptor-mediated radionuclide therapy.

Methods. A receptor imaging and treatment study was initiated in Europe, "MAURITIUS" (Multicenter Analysis of a Universal Receptor Imaging and Treatment Initiative, a eUropean Study). In this study, patients with tumors known to express one of the hSSTR subtypes undergo ^{111}In-DOTA-lanreotide scintigraphy (150 MBq; 10 nmol peptide). Dosimetry calculations are performed for tumor lesions and major organs. In patients with a calculated tumor dose of >10 Gy/GBq, ^{90}Y-DOTA-lanreotide treatment is initiated using a standard dose of 1 GBq (50 nmol peptide). Treatment is repeated every 4th week. A cummulative dose of 7 GBq has been administered so far. Treatment results are evaluated by conventional imaging techniques including CT, MRI, FDG-PET as well as repeated ^{111}In-DOTA-lanreotide scintigraphy / dosimetry. Patients are monitored for quality of life improvement, as well as side effects.

Results. ^{111}In-DOTA-Lanreotide scintigraphy / dosimetry indicated a tumor dose of up to 100 Gy/GBq ^{90}Y-DOTA-lanreotide, despite that most tumor lesions were calculated to receive a dose of 5 - 25 Gy/GBq. In none of >100 tumor patients scanned with ^{111}In-DOTA-lanreotide, side effects were recorded. In most patients, at least one known tumor site was indicated by ^{111}In-DOTA-lanreotide. ^{90}Y-DOTA-lanreotide treatments were given to 20 tumor patients with either de-differentiated radioiodine-negative thyroid cancer, neuroendocrine tumors, lymphomas, or adenocarcinomas. At study entry, all patients had progressive tumor disease under conventional therapy. Most patients were heavily pretreated by chemotherapy and/or external radiotherapy, and receptor-mediated radionuclide therapy was chosen as an experimental end-stage intervention. In roughly 50% of patients, stable disease, in 25% regressive, and in 25% progressive disease was recorded. No acute or chronic severe hematological toxicity, change in renal or liver function parameters due to ^{90}Y-DOTA-lanreotide, was reported.

Conclusions: ^{111}In-DOTA-lanreotide shows a high tumor uptake for a variety of different human tumor types, has a favorable dosimetry and is clinically safe. ^{90}Y-DOTA-lanreotide is a promising novel receptor radiotherapeutical in the treatment of progressive thyroid cancer, certain neuroendocrine tumors or lymphomas. However, optimal dose, dose regimen, duration of treatment, time of inclusion of a patient, etc. are not known at present.